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EXAMINER I012CN

ART UNIT	PAPER NUMBER
1814	39

18M2/0624

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FRAMINGHAM, MA 01701

DATE MAILED: 06/24/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☐ This application has been examined ☒ Responsive to communication filed on 1-18-96 & 4-15-96 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 202-223 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☒ Claims 1-201 have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 202-219, 221-223 are rejected.

5. ☒ Claims 220 are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and the finality of that action is withdrawn.

Since this application is eligible for the transitional procedure under 37 CFR 1.129(a) and since the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.129(a). Applicants first submission filed January 18, 1996, Paper #37, has been entered.

This Office Action is in response to Paper #37 (filed January 18, 1996), and Paper #38 (filed April 15, 1996). Claims 1-201 have been cancelled. Claims 202-223 are currently pending and under examination.

Due to the cancellation of the previously examined Claims, previous rejections are withdrawn and somewhat restated below in view of the newly added Claims. Applicants arguments against the rejections are addressed.

Withdrawal of Objections and Rejections

The objection to the disclosure for using acronyms within the Claims is withdrawn.

The rejection of the Claims under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to DNA encoding huCFTR having the sequence set forth in Table 1, the intron or intervening sequence set forth in Fig. 6, point mutations T748C with A774G and T936C alone, and low copy number plasmids is withdrawn.

Paper #38 addressed these issues which are now moot in view of the newly added Claims. No arguments were presented in Paper #39.

New Rejections

Claims 206-211, 213, 215, 218, and 223 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 206 is confusing because a fusion protein is being described but not readily claimed because the first sequence must encode CFTR but the second sequence begins at position 907 within the first sequence. Claim 206 may be made more clear if amended to say that the wild-type sequence has a second non-natural sequence within it. For example, "A purified and isolated DNA molecule capable of propagation in E. coli, said DNA consisting of cDNA encoding wild-type CFTR having a second non-natural DNA sequence being located within this cDNA encoding wild-type CFTR being located downstream from nucleotide position 907 and wherein said second sequence disrupts the expression of CFTR fragments toxic to E. coli". Claim 218 is indefinite because it is not clear what is essential about the plasmid. The term "consisting essentially of" is used to describe compositions nad not compounds; therefore, Applicants may wish to use the terms "having" or comprising. Additionally, Claim 218 appears to read that the DNA includes a plasmid, but a plasmid is generally regarded as being complete without addtional DNA.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 202, 205, 212, 216, 217, and 222 are rejected under 35 U.S.C. § 102(e) as being anticipated by Collins (USP 5,240,846). In Example 1, Collins teaches that prokaryotic transcription from internal CFTR cDNA sequences may result in the expression of a protein that is toxic to the bacteria, resulting in early attempts to reconstitute a full-length CFTR cDNA from overlapping clones unsuccessful. Collins introduced three silent mutations at T930C, A933G, and T936C (Claim 202), and these mutations ablated the toxic effect in the bacteria by potentially interfering with the cryptic promoter. The enabled the reconstruction of a contiguous CFTR cDNA sequence (Claim 205). Though Collins does not expressly state that this CFTR cDNA was placed in a plasmid, such could not be accomplished without the placement of the CFTR in a plasmid and therefore the placement of the cDNA CFTR into a plasmid is inherent to the reconstitution of the full-length cDNA encoding CFTR (Claim 212). Figure 2 shows an RNA blot analysis of this CFTR containing the three silent mutations. Therefore, RNA complementary to this cDNA encoding CFTR is taught by Collins (Claim 222). Collins teaches that pLJ-CFTR clones have one copy of provirus per CFPAC-1 cell (col. 8, lines 43-47). Therefore, cDNA encoding CFTR and an origin of replication (from pBR) resulting in low copy number is taught in Collins (Claims 216, 217).

It has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchison*, 69 USPQ 138.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 203, 204, 214, 219, and 221 are rejected under 35 U.S.C. § 103 as being unpatentable over Collins (USP 5,240,846). The teachings of Collins are set forth above. Collins additionally teaches that the cryptic prokaryotic promoter is an E. coli promoter (col. 11, line 45). It would have been obvious to a person of ordinary skill in the art to place a single point mutation at any one of the bases taught by Collins because one skilled in the art would reasonably expect that the disruption of the cryptic prokaryotic promoter would result in reduced or ablated toxicity in bacteria upon expression in prokaryotic cells (Claims 203, 204). Because the cryptic prokaryotic promoter is taught by Collins to be an E. coli promoter and because the modified form of the cDNA encoding CFTR shown to ablate toxicity in bacteria was placed in the pLJ having low copy number, it would have been obvious to a person of ordinary skill in the art to infect E. coli with this retrovirus pLJ-CFTR because one would reasonably expect that the E. coli would not experience a toxic effect after introduction of this modified cDNA encoding CFTR as taught by Collins et al. for an undefined bacteria (Claims 214, 219, and 221).

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Art Unit 1814

Claim 220 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 202, 205, 212, 216, 217, 218, and 222 would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. § 112.

As allowable subject matter has been indicated, applicant's response must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 C.F.R. § 1.111(b) and section 707.07(a) of the M.P.E.P.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D., whose telephone number is (703) 308-0034. The Examiner can normally be reached Monday through Thursday from 7:00 A.M. to 4:30 P.M. The Examiner can also be reached on alternate Fridays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Robert A. Wax, can be reached at (703) 308-4216. The fax phone number for Group 1800, AU 1814, is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

kcc
6-11-96

ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
GROUP 180